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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/627,383	07/28/2000	Paul T. Matsudaira	0399.1211-001	3215

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/03/2004 20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/627,383	Applicant(s) MATSUDAIRA ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election Restriction Requirement

1. Applicant response to the Restriction Requirement dated April 22, 2003 is acknowledged (Paper #19 filed 10/2/03). Applicant traversed the restriction requirement because the claims were previously considered. Although the claims were amended, Examiner has found the arguments persuasive. The restriction requirement set forth in paper #17 is vacated. Currently claims 11-15 and 27-29 are under consideration.

Amendment Entry

2. Applicants' response to the Office Action mailed 30 July 2002 in Paper #12, filed 2/4/03 is acknowledged. In amendment-C filed therein claims 11, 14, 27, and 29 were modified.

OBJECTIONS WITHDRAWN

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

4. The information disclosure statement filed 3/22/01-Paper #6, has been considered as to the merits prior to first action. Further application number 60/061,801 filed 10/14/97 has been considered and indicated on page 2 of paper #6 filed 3/22/01.

5. The Supplemental disclosure statement filed 2/4/03 on Paper #16 has been considered as to the merits before Final Action.

OBJECTIONS MAINTAINED

Drawings

6. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

NEW OBJECTIONS

Request for Corrected Filing Receipt

7. Applicants request to correct an error/inconsistency in priority data regarding provisional application no. 60/061,801 filed 10/14/97 is noted. Application number 60/061,801 filed 10/14/97 has been deleted in the continuing data as claimed by applicant.

Specification

8. The first line of the disclosure should be updated. The benefit to application number 60/061,801 should be omitted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 11, 14, 27 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case does not set forth any all possible mutations (detections and/or substitutions) to the GFP nucleic acid of the instant claims therefore the written description is not commensurate in scope with the claims.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the detailed structure of the encompassed all possible GFP nucleic acid mutations and the unlimited number of sequence configurations encompassed by the claims and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. (Please see instant disclosure page 13-15). The sequence of the structure itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of a compound/seq.id/etc. by only their functional activity does not provide an adequate written description of the genus.

The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules, usually defined by a sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". The disclosure provides insufficient support to the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

10. Claims 11, 14, 27 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide description of or enablement for any and every modified GFP nucleic acid sequence which is mutated.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant provides guidance for specific embodiments covered by the seq id nos identified in the disclosure however the disclosure does not provides guidance as to all modifications or structures encompassed by the broad claims.

The predictable structure ad function of the unlimited possible modifications to a GFP nucleic acid may exhibit very different structures not necessarily having with the same specificity. For example, very different V_H chains can combine with the same V_L chain to produce binding sites with nearly the same size, shape, antigen specificity, and affinity.

A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found to have different specificities.

In the absence of any guidance other than to the use of the sequences taught in the instant specification, one would not know or be able to predict ány and all possible structures or modifications were important/read on the instant claims and the amount of experimentation required to determine the same combination of the structures would be undue. Note that an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable.

Response to Arguments

Applicants contend that the skill and knowledge at the time of application filing was high with respect to GFP. The GFP protein has been sequenced and mutants or modification to the protein are taught in the prior art.

This argument was carefully considered, but not found persuasive because an infinite number of mutants and or modification to the known GFP protein exist. Accordingly applicant is in possession of the constructs set forth in the disclosure but not any and all possible mutants derived/produced therefrom. The rejections are maintained.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

I. Claims 11 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al. (US Patent #6,180,343).

Anderson et al. teach fusion constructs of GFP. The protein is modified to include random and defined peptides (control sequences) to increase cellular expression levels, decrease the cellular catabolism, increase the conformational stability relative to linear peptides, and to increase steady state concentrations (tailor sensitivity). The preferred areas of modification involved the loops at amino acid positions 130 to 135, 154 to 159, 172 to 175, 188 to 193, and 208 to 216. Applicant modifications are between 157 and 158 or 172 and 173. These areas include sites for restriction (end nuclease restriction sites). Accordingly the sites indicated by Applicant are inherent to the teaching of US patent #6,180,343 which discloses the same regions.

The patent further discloses nucleic acid sequences encoding the fusion proteins along with vectors. See column 1 line 65 through column 2 line 23.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US Patent #6,180,343) in view of Gorman et al. (WO 99/19489).

Please see Anderson et al. as set forth above.

Anderson et al. differ from the instant invention in not specifically disclosing sequence identification number 1.

However, Gorman et al. (WO 99/19489) disclose a composition comprising the specific sequence identification number 1 as Myosin IXa polypeptide sequence identification number 1. See abstract and pages 4-5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize various modified GFP sequences as taught by Anderson et al. and include sequence identification number 1 as taught by Gorman et al. because Gorman et al. taught that sequence identification number 1 (Myosin IXa activity) is involved in several immunological events (ATP binding, ATPase, zinc binding, calmodulin/EF binding, G-coupled receptors, membrane binding, modulation of cell interacts, calcium release, cytoskeletal rearrangements, etc.-see page 10-11). Gorman et al. further disclose that expression vectors wherein Myosin IXa (seq id no 1) is linked to a signal sequence for selected markers are convenient. See page 18-22, esp page 21 line 20-28.

II. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US Patent #6,180,343) in view of in view of Gorman et al. (WO 99/19489) and in further view of Kimata et al. (Biochemical and Biophysical Research Communications, 232, 69-73, 1997).

Please see Anderson et al. as set forth above.

Anderson et al. differ from the instant invention in not specifically teaching the substitution of Ser at the 147 position to Proline (S147P) in GFP.

Kimata et al. disclose this limitation. See abstract and pages 71 through 73.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize various modified GFP sequences as taught by Anderson et al. and substitution of Ser at the 147 position to Proline (S147P) as taught by Kimata et al. because Kimata et al. taught that this substitution emits a stronger fluorescent signal at higher temperatures. See abstract.

III. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US Patent #6,180,343) in view of Gorman et al. (WO 99/19489).

Please see Anderson et al. as set forth above.

Anderson et al. differ from the instant invention in not specifically disclosing sequence identification number 1.

However, Gorman et al. (WO 99/19489) disclose a composition comprising the specific sequence identification number 1 as Myosin IXa polypeptide sequence identification number 1. See abstract and pages 4-5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize various modified GFP sequences as taught by Anderson et al. and include sequence identification number 1 as taught by Gorman et al. because Gorman et al. taught that sequence identification number 1 (Myosin IXa activity) is involved in several immunological events (ATP binding, ATPase, zinc binding, calmodulin/EF binding, G-coupled receptors, membrane binding, modulation of cell interacts, calcium release, cytoskeletal rearrangements, etc.-see page 10-11).

Gorman et al. further disclose that expression vectors wherein Myosin IXa (seq id no 1) is linked to a signal sequence for selected markers are convenient. See page 18-22, esp page 21 line 20-28.

III. Claims 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US Patent #6,180,343) in view of in view of Gorman et al. (WO 99/19489) and in further view of Kimata et al. (Biochemical and Biophysical Research Communications, 232, 69-73, 1997).

Please see Anderson et al. in view of Gorman et al. (WO 99/19489) as set forth above.

Anderson et al. in view of Gorman et al. differ from the instant invention in not specifically teaching the substitution of Ser at the 147 position to Proline (S147P) in GFP.

Kimata et al. disclose this limitation. See abstract and pages 71 through 73.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize various modified GFP sequences as taught by Anderson et al. in view of Gorman et al. and substitution of Ser at the 147 position to Proline (S147P) as taught by Kimata et al. because Kimata et al. taught that this substitution emits a stronger fluorescent signal at higher temperatures. See abstract.

Response to Argument

Applicant's arguments against the references of record were considered and found persuasive, accordingly new references have been cited against the amended claims.

15. For reasons aforementioned, no claims are allowed.

Remarks

16. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

Tsien et al. (WO 92/00388) teach long wavelength engineered fluorescent proteins and their methods of use. Fluorescent molecules are attractive as reporter molecules in many assay systems because of their high sensitivity and ease of quantification (page 1, lines 15-16).

Thastrup et al.(US patent 5,958,713) disclose modified GFP proteins to detect biological activity.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Lisa V. Cook
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4/30/04

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